PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 07-1008-WO-US)

In the Application of:		
	Alastair David G. Lawson et al.	Examiner: Joanne Hama
Serial No.:	10/578,384	Group Art Unit: 1632
Filing Date:	January 16, 2007	Confirmation No. 1913
For:	Methods for the Treatment of Inflammatory Bowel Disease	

DECLARATION OF ALASTAIR DAVID G. LAWSON, DIANE MARSHALL AND TIMOTHY BOURNE UNDER 37 C.F.R. § 1.131

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

I, Alastair David G. Lawson and I Timothy Bourne and I Diane Marshall, in support of the above-identified United States patent application, do declare and state as follows:

1. We are the first, original, and joint inventors of the subject matter claimed in United States Patent Application Serial No. 10/578,384, filed on January 16, 2007, and entitled "Methods for the Treatment of Inflammatory Bowel Disease," which claims priority benefit of International Application PCT/GB04/04652 filed November 3, 2004, which claims the benefit of Great Britain application 0325836.5 filed November 5, 2003. We submit this Declaration to overcome the Section 102(e) rejection of this patent application based on United States Patent Publication US 2005/0059113 to Bedian et al. (hereinafter "Bedian"), which was filed on September 9, 2004 and claims priority to U.S. Provisional Patent Application No. 60/502,163, filed on September 10, 2003 (the priority

date of Bedian). The Bedian application issued September 22, 2009 as U.S. Patent No. 7,592,430.

2. We, at all relevant times herein, were and remain employees of Celltech R&D Limited, of 208 Bath Road, Slough, Berkshire, SL1 3WE, United Kingdom, predecessor-in-interest of the current assignee of this application, UCB Pharma S.A., 60 Allee de la Recherche, Brussles, Belgium.

3. We conceived the inventions disclosed in the above-reference patent application well prior to September 10, 2003 (the priority date of Bedian). We also exercised diligence in reducing our inventions to practice from at least prior to September 10, 2003, with both actual construction to practice as set forth in Exhibit 1 appended hereto, and continuing through to the constructive reduction to practice evidenced by filing the original Great Britain patent application on November 5, 2003.

4. Accompanying this Declaration is Exhibit 1, which evidences our efforts to diligently reduce the inventions to practice prior to that September 10, 2003.

5. Exhibit 1 is a copy of selected pages of laboratory notebook No. 10015850 (maintained by Dr. Diane Marshall). The pages of the notebook included in Exhibit 1 are the cover, Accession page, the Table of Contents page (partially redacted), and pages 1-30 and 53-67. These are the pages in the notebook relating to the use of anti-CSF-1 antibody as a treatment for DSS-induced colitis in mice. The dates on the pages of the notebook in this Exhibit have been redacted. Each original page of the notebook included two dates, one in the upper right-hand corner and one in the lower right-hand corner. The date in the upper right-hand corner represented the date that the experiment was conducted. The date in the lower right-hand corner represented the date that the various graphs and data sheets were physically affixed in the notebook. The upper-right hand corner dates of said pages are all dated prior to September 10, 2003. The lower right-hand corner dates of pages 1-30 and 53-59 are all dated prior to September 10, 2003.

6. The currently amended claims of the present application relate to a method for the treatment of inflammatory bowel disease (IBD) comprising administering a therapeutically effective amount of an inhibitor of CSF-1 activity to a patient in need thereof, wherein said inhibitor of CSF-1 activity is selected from one or more of an anti-CSF-1 antibody, or a CSF-1-binding fragment of an anti-CSF-1 antibody. This subject matter is reflected in the work recorded in Exhibit 1. At page 1, it is reported that anti-CSF-1 antibody significantly reduced disease severity of DSS-induced colitis in mice, as noted by reduced loss of body weight, less colonic shortening, reduced colonic disease symptoms (diarrhea, blood, profuse bleeding) reduced clinical disease scores (colonic disease and weight loss), reduced number of $CD3^+$ cells and neutrophils in the colon. Graphs in the Exhibit illustrating this work correspond to the figures of the present patent application. Thus, application Fig. 1 corresponds to the top figure on page 2 of Exhibit 1; application Fig. 2 corresponds to the bottom figure on page 2 of Exhibit 1; application Fig. 3a corresponds to the top figure on page 3 of Exhibit 1; application Fig. 3b corresponds to the bottom figure on page 3 of Exhibit 1; application Fig. 4a corresponds to the top figure on page 4 of Exhibit 1; application Fig. 4b corresponds to the bottom figure on page 4 of Exhibit 1; application Fig. 5 corresponds to the figure on page 22 of Exhibit 1; and application Fig. 6 corresponds to the bottom figure on page 26 of Exhibit 1. Each of these pages in the original is dated in the upper right-hand corner with a date prior to the September 10, 2003 priority date of the Bedian reference.

7. All of the work referred to in this declaration occurred in the United Kingdom, except the filing of the present application which occurred in the United States through our patent counsel, Woodcock Washburn.

8. We hereby acknowledge that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under

Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 9th October 2009

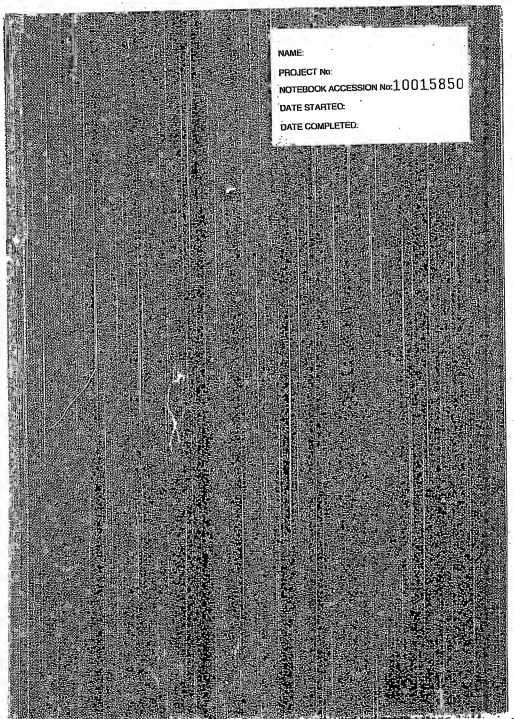
Alastair David G. Lawson

Date: 9th October 2009

Timothy Bourne

Date: 9/10/09
9th October 2009

Diane Marshall


NAME:
PROJECT No:
NOTEBOOK ACCESSION No:10015850
DATE STARTED:
DATE COMPLETED:

REDACTED

ACCESSION PAGE

1. This Notebook and all data recorded therein are the property of CELLTECH R & D LIMITED. All contents are strictly confidential. The Notebook must be returned to the company upon completion, upon request, or upon termination of employment.

2. The persons to whom this Notebook is assigned must take every precaution to safeguard against loss. In the case of fire, theft, or disappearance of this Notebook, the employee must immediately notify their Head of Department. A written report describing the circumstances of the loss must follow.

3. All persons using the Notebook and their line manager must give a specimen signature in the relevent section below.

4. Full details on how to complete the Notebook are available in the relevent procedure; 'R & D Notebook Record Keeping (Non-GLP Studies)' procedure (for Non -GLP)/ SOP No. GLP-SOP-MAN-16 (for GLP).

PROJECT TITLE: GENERIC 113.0

GLP STUDY: YES/(NO) NOTEBOOK NO: 20.0/38.30

ASSIGNED TO : D MARSHALL DATE OF ISSUE:
(SCIENTIST NAME(S))

CONTINUED FROM NOTEBOOK NO: DATE:

CONTINUED TO NOTEBOOK NO: DATE:

INSPECTED BY: DATE:
(Line Management)

TO BE COMPLETED BY ALL NOTEBOOK SIGNATORIES.

NAME (PRINTED)	SIGNATURE	INITIALS	DATE

PRINTED AND PRODUCED BY THAMES VALLEY PRINTERS 01628 631130

REDACTED

DATE

TABLE OF CONTENTS

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TITLE: Anti-CSF-1 in DSS-induced colitis in mice. | PAGE No. 1

DATE
PROJECT NO
NOTEBOOK NO 10015 850

- DSS model of IBD (mice).

Aim
To assess the effects of anti-CSF-1 antibody on DSS induced colitis in mice.

Procedure
Licence 7057/48, procedure 18.
Balb/c mice (males, batch RM3305, arrived [redacted] 18-24g) weighed and injected subcutaneously with mAb @ 10mg/kg.
Group 1 – 101.4, control antibody (lot- 10014426/15) – (r1 isotype)
Group 2 – Anti-CSF-1, alkylated Ab33 (4.7mg/kg)
10 mice in each group. Normal drinking water then replaced with 1% DSS (ICN MW 36-50K, Cat No 160110) in tap water 24 hours after 1st antibody injection. 10 x 4 43g 9F

Group 3 – No treatment control group
10 mice will continue to have normal drinking water.

Mice will receive antibody once a week. Animals will be weighed each day and signs of disease (loose stools, bleeding) noted. The volume of 1% DSS or water consumed also measured by weight. At end of expt., colons will be removed and length measured. A 1 cm section will be collected from the distal end for assessment of neutrophil and T cell infiltration by FACS analysis. The next 2 cm section will be collected and placed in formalin for histological analysis. The next cm will be place in culture medium for 24 hours, after which time the supernatant will be collected and cytokine levels measured by luminex. Plasma will also be collected at termination.

Study Period

10015850/1
D. Wescott

The anti-CSF1 antibody significantly reduced disease severity of DSS-induced colitis in mice, as seen by reduced loss of body weight, less clinical scoring, reduced clinical disease symptoms (Diarrhoea, Rectal prolapse Bleeding), reduced distal disease scores (clinical disease + weight loss), reduced numbers of CD3+ cells and neutrophils in the colon (these results were all significantly reduced by FACS analysis, but colons taken and given to Trevor for immunohistochemistry, which often lightens up the data)

Raw data in NB. 10017550

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BY: ..... | RECORDED BY D. Wescott DATE

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TITLE: anti-CSF-1

PAGE No. 2

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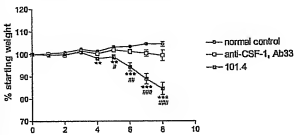
PROJECT NO

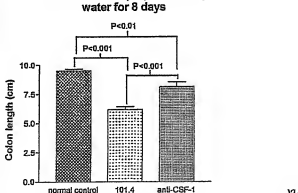
NOTEBOOK NO 10015850

Effect of anti-CSF-1 Ab on body weights of mice after addition of DSS (1%) in drinking water



n = 10. Antibodies injected weekly at 10mg/kg sub cut., 1st injection 24hrs before addition of 1% DSS to drinking water
Statistical analysis by ANOVA with Bonferroni's post test-
** P<0.01, *** P<0.001 101.4 vs normal animals
# P<0.05, ## P<0.01, ### P<0.001 101.4 vs anti-CSF-1
No significant difference between anti-CSF-1 and normal animals

Effect of anti-CSF-1 Ab on colon length of mice after addition of DSS (1%) in drinking water for 8 days



n = 10. Antibodies injected weekly at 10mg/kg sub cut., 1st injection 24hrs before addition of 1% DSS to drinking water
Statistical analysis by ANOVA with Bonferroni's post test

10015850/2 D. Thackray

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TITLE: anti-CSF-1

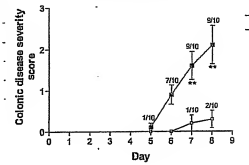
PAGE No. 3

DATE

PROJECT NO

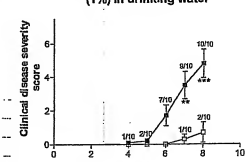
NOTEBOOK NO 10015850

Effect of anti-CSF-1 Ab on colonic disease severity score of mice after addition of DSS (1%) in drinking water



Disease scored: 1 = soft faeces/diarrhoea; 2 = signs of blood in guiffaces; 4 = profuse bleeding from anus.
**, P<0.01 analysed by Mann Whitney

Effect of anti-CSF-1 Ab on clinical disease severity score of mice after addition of DSS (1%) in drinking water



Disease scored as gut disease score plus weight loss score:-
gut disease score: 1 = soft faeces/diarrhoea; 2 = signs of blood in guiffaces; 4 = profuse bleeding from anus
weight loss score: += 5-10%; 2= 10-15%; 4= 15-25% weight loss
**, P<0.01; ***, P<0.001 analysed by Mann Whitney

10015850/3 D. Thackray

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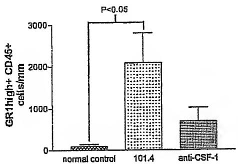
TITLE: anti - CSF-1 PAGE No. 4

DATE
PROJECT NO
NOTEBOOK NO 10015850

GR1high+ CD45+ cells/mm in LP population from colons of mice on day 8 after DSS (1%)



n = 10. Antibodies injected weekly at 10mg/kg sub cut., 1st injection 24hrs before addition of 1% DSS to drinking water Statistical analysis by ANOVA with Bonferroni's post test.

anti-CD45-Cychrome
cat n° 553082 lot n° M074786

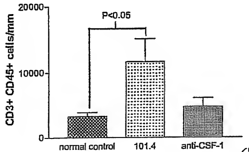
anti-GR-1 PE cat n° 553128
lot 0000037234

anti-CD3-FITC cat n° 553062
lot 0000049631

control Abs rat 2bPE
cat n° 559529 lot n° 0000 29...

hamster IgG1 FITC cat n° 553953
lot n° M071190

CD3+ CD45+ cells/mm in LP population from colons of mice on day 8, after DSS (1%)



10015850/4 D. MacDonald

n = 10. Antibodies injected weekly at 10mg/kg sub cut., 1st injection 24hrs before addition of 1% DSS to drinking water Statistical analysis by ANOVA with Bonferroni's post test.

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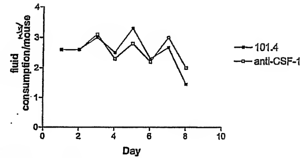
BY........ ..../..../.... RECORDED BY D. MacDonald DATE

TITLE: anti - CSF-1 PAGE No. 5

DATE
PROJECT NO
NOTEBOOK NO 10015850

Fluid consumption after addition of DSS (1%) in drinking water



D. MacDonald 10015850 P5

(CSF-1).pzm:Data Table-colon length

	A	B	C
	101.4	anti-CSF-1	normal contro
	Y	Y	Y
1	7.60	8.30	9.40
2	5.80	8.50	9.60
3	6.60	5.50	9.30
4	5.40	8.60	9.50
5	8.10	8.50	10.70
6	5.20	9.00	9.20
7	8.00	6.70	9.00
8	5.90	7.90	9.50
9	8.00	9.00	9.30
10	7.10	9.50	9.60

D. MacDonald 10015850/5

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BY........ ..../..../.... RECORDED BY D. MacDonald DATE

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TITLE: anti-CSF-1

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DATE
PROJECT NO
NOTEBOOK NO 10015850

Cage 1 - DSS + 101.4 — mouse weights, animal number

day	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	22.2	24.8	25.3	25.8	23.6	23	22.9	23.1	22.4	24.5	23.76	1.257157	0.397835
1	21.8	25	24.7	25.5	23.8	23.1	23	23.3	22.4	24.4	23.80	1.225033	0.387922
2	21.7	25.1	25.1	25.7	23.1	23.3	22.9	23.7	22.5	24.6	23.77	1.303031	0.412351
3	21.7	25.1	25.3	26.3	23.9	24.1	23.3	23.5	21.9	24.8	23.98	1.464959	0.463607
4	21.3	24.6	24.0	25.8	23	23.2	23	22.7	21.1	24.3	23.34	1.454649	0.460332
5	21.7	25	24.6	24.4	22.2	23.5	23.1	23.8	20.9	24.6	23.48	1.342303	0.424779
6	21.8	24.7	24.4	22	22.3	21.3	22.8	22.4	18.5	23.9	22.41	1.704159	0.564607
7	21.3	24.2	22.7	20.4	20.9	19.8	22.1	20.3	17	22.5	21.14	2.01836	0.638722
8	20.9	23.5	21.3	18.8	20.4	16.3	21.3	18.9	15.6	22	20.1	2.245984	0.710754
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11											#DIV/0!	#DIV/0!	#DIV/0!

DSS + anti-CSF-1, Ab33 — animal number

day	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	24.4	24.2	21.4	24.8	25.7	24.8	25.7	25.3	24.8	24.4	24.51	1.217876	0.385404
1	24.3	24.5	21.7	24.2	25.9	24.8	25.9	25	25.1	24.2	24.54	1.182464	0.374198
2	24.4	24	21.3	24.1	25.6	24.4	25.2	25.3	25.1	24.6	24.4	1.214724	0.384408
3	24.5	23.9	21.8	25.2	26.[illegible]	25.1	23.4	25.9	25.6	25	24.89	1.244053	0.393804
4	24.6	23.4	22.1	25.1	25.4	23.9	25.2	25.9	25.2	24.8	24.56	1.130585	0.35779
5	25.4	23.2	22.1	26.8	26.3	24.5	25.5	26.4	25.7	25.1	25	1.378405	0.436204
6	25.4	23.6	21.3	25.8	26	24.5	24.9	25.8	25.8	25.3	24.82	1.432791	0.453415
7	25.4	24.3	19.4	24.0	20.3	25.1	24.5	25.7	25.9	25.2	24.68	1.946903	0.616741
8	25.6	24.1	17.8	25.3	26.2	25.2	23.2	25.6	20.2	25.3	24.43	2.566638	0.812859
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10											#DIV/0!	#DIV/0!	#DIV/0!
11											#DIV/0!	#DIV/0!	#DIV/0!

control — animal number

day	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	25.7	27.3	25.3	23.9	25.3	23.8	24.8	26.1	21.8	23.6	24.67	1.786085	0.566100
1	26.3	27.5	25.1	23.3	25.6	23.4	24.3	26.8	22	23.6	24.77	1.739784	0.550558
2	26	27.4	25.4	23.5	25.8	23.5	24.7	26.6	22.1	23.7	24.87	1.654657	0.523820
3	26.6	27.8	26	23.7	26.2	23.8	24.7	27.3	22.1	24.2	25.22	1.709973	0.540447
4	26.0	27.2	25.7	23.5	26.2	23.5	24.5	26.8	21.9	24	25.01	1.782913	0.564213
5	27	28	26.3	24.2	26.6	23.9	24.8	27	22.5	24.2	25.47	1.75249	0.554585
6	26.8	28.1	26.2	24	28.8	24.2	25.1	27.4	22.2	24.2	25.51	1.845987	0.584173
7	27.4	28.4	26.4	24.8	26.8	24.8	25.4	27.2	22.5	24.6	25.81	1.750208	0.553563
8	26.9	28	26.4	24.4	26.8	25.7	25.6	27.4	22.2	24.5	25.77	1.7[illegible]83	0.540564
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TITLE: anti-CSF-1.

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DATE
PROJECT NO
NOTEBOOK NO 10015850

Cage 1 - DSS + 101-4 — mouse weights as % of starting weight, animal number

day	1	2	3	4	5	6	7	8	9	10	average	sd	sem
1	100	100	100	100	100	100	100	100	100	100	100	0	0
2	97.2973	100.8065	97.82846	88.03721	100	100.4348	100.4367	100.8658	100	99.59184	98.50985	1.221263	0.402298
3	97.74775	101.2097	99.20949	99.0124	97.88136	101.3043	100	102.5974	100.4464	100.4002	100.0417	1.512704	0.478723
4	97.74775	101.2097	100	101.038	100.8475	104.7826	101.7467	101.7316	97.76786	101.2245	100.0990	2.06348	0.653
5	95.94595	99.19355	97.2332	99.22481	97.45763	100.6098	100.4367	98.2684	94.19643	99.18367	98.20089	2.047604	0.647870
6	97.74775	100.0065	97.2332	94.57364	88.30508	102.1739	100.8734	102.1045	93.30357	101.2245	98.6406	3.140583	0.993855
7	99.1987	99.59677	98.44269	85.27132	94.40153	92.6087	99.56332	95.9897	82.58929	97.55102	94.32825	5.914098	1.87155
8	95.94595	97.58065	80.72332	78.06977	88.55932	85.21739	98.50655	87.87879	75.80286	93.46939	88.9844	7.340028	2.322704
9	94.14414	94.76806	84.16972	72.88022	88.44068	79.66522	93.0131	81.81918	69.64286	89.79592	84.82301	8.75623	2.770959
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11											#DIV/0!	#DIV/0!	#DIV/0!
12											#DIV/0!	#DIV/0!	#DIV/0!

DSS + α-CSF-1 — animal number

day	1	2	3	4	5	6	7	8	9	10	average	sd	sem
1	100	100	100	100	100	100	100	100	100	100	100	0	0
2	99.59016	101.2397	101.4819	88.37398	100.7782	99.19355	100.7782	98.81423	102.0325	99.10033	100.1383	1.255802	0.397400
3	100	99.17355	99.53271	97.96748	99.61009	98.3871	98.05447	100	102.0325	100.8197	99.65784	1.265718	0.400544
4	102.0492	98.76033	101.8692	102.439	101.5564	101.2097	98.03268	102.3715	104.065	102.459	101.5612	1.641434	0.519441
5	100.8197	98.60421	103.271	102.0025	98.83268	96.37097	98.05447	102.3715	102.439	101.6393	100.2525	2.5487	0.805918
6	104.0984	95.66777	103.271	104.878	102.3346	98.79032	99.22179	104.3478	104.4715	102.6589	102.015	3.026035	0.957000
7	104.0984	97.52066	99.53271	104.878	101.1673	98.79032	98.88716	101.1858	104.878	103.6885	101.2827	2.024638	0.657163
8	104.0984	100.4132	90.65421	100.813	102.3346	101.2097	95.33874	101.581	105.2846	103.2787	100.4908	4.376272	1.384696
9	104.918	99.67678	82.24299	102.8455	101.8455	101.6129	90.27237	101.1858	106.5041	100.6855	99.46025	7.476801	2.360709
10											#DIV/0!	#DIV/0!	#DIV/0!
11											#DIV/0!	#DIV/0!	#DIV/0!
12											#DIV/0!	#DIV/0!	#DIV/0!

normal control — animal number

day	1	2	3	4	5	6	7	8	9	10	average	sd	sem
1	100	100	100	100	100	100	100	100	100	100	100	0	0
2	99.50167	100.7326	99.60317	98.14694	101.1858	103.5398	98.78049	101.9157	100.9174	100	100.4328	1.553735	0.491680
3	97.37828	100.3663	100.7937	100	101.9763	103.8823	100.4065	101.9157	101.3761	100.4237	100.8619	1.685008	0.532848
4	99.62547	101.0989	103.1746	100.8511	100.5573	105.3097	100.4065	104.5977	101.3761	102.5424	102.254	1.801349	0.569364
5	100.3745	99.6337	101.9841	100	103.6573	103.8823	99.5935	102.682	100.4587	101.6949	101.3001	1.621008	0.512250
6	101.1236	102.5641	104.3651	102.9787	105.1383	105.7522	101.2195	103.4483	103.211	102.9661	103.2767	1.504553	0.476128
7	100.3745	102.9304	103.9683	102.1277	105.0288	107.0796	102.0325	104.9808	101.8349	102.9661	103.4228	2.001624	0.632413
8	102.6217	104.0293	104.7619	104.6809	105.0288	108.8496	103.252	104.2146	103.211	105.0847	104.6035	1.769889	0.560028
9	100.7491	102.5641	104.7919	103.0298	105.1383	113.7168	104.065	104.9808	101.0349	100.8130	104.5458	3.522405	1.114665
10	0										0	#DIV/0!	#DIV/0!
11	0										0	#DIV/0!	#DIV/0!
12	0										0	#DIV/0!	#DIV/0!

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Sample #	Dead Cow Count	Dead Cow Count / ul	Vol aspirated	Event cow Cells / FACS	Cells / sample	Cells / mg	Cells / mm	Sample wt (mg)	Sample length (mm)	mg/mm
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Sample #	Dead Cow Count	Dead Cow Count / ul	Vol aspirated	Event cow Cells / FACS	Cells / sample	Cells / mg	Cells / mm	Sample wt (mg)	Sample length (mm)	mg/mm
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

D. McNall 10015850 P8

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Marino DSS - July03.1 Fluid consumption

Cage 1 - DSS + 101.4

Day	New weigh	Weight aft	Difference	Diff - 1ml	Amnt per mouse (ml)
0		469			
1	442	442	27	20	2.6
2	415	415	27	20	2.6
3	304	416	31	30	3
4	300	390	20	25	2.5
5	350	338	34	33	3.3
0	314	314	24	23	2.3
7	280	341	25	24	2.666667
8	327		14	13	1.444444
9			0	-1	-0.111111
10			0	-1	-0.111111
11			0	-1	-0.111111
12			0	-1	-0.111111
13			0	-1	-0.111111

Cage 2 - DSS + anti-CSF-1, Ab33

Day	New weigh	Weight aft	Difference	Diff - 1ml	Amnt per mouse (ml)
0		431			
1	404	404	27	28	2.8
2	377	377	27	20	2.0
3	345	422	32	31	3.1
4	398	398	24	23	2.3
5	300	328	20	28	2.0
6	297	297	23	22	2.2
7	209	340	28	27	3
8	327		19	10	2
9			0	-1	-0.111111
10			0	-1	-0.111111
11			0	-1	-0.111111
12			0	-1	-0.111111
13			0	-1	-0.111111

Cage 3 - control (9 mice)

Day	New weigh	Weight aft	Difference	Diff - 1ml	Amnt per mouse (ml)
0		623			
1	601	601	22	21	2.1
2	578	570	25	24	2.666667
3	548	568	28	27	3
4	542	542	24	23	2.555556
5	514	504	20	27	3
0	639	639	25	24	2.666667
7	512	542	27	26	2.888889
8	510		24	23	2.555556
9			0	-1	-0.111111
10			0	-1	-0.111111
11			0	-1	-0.111111
12			0	-1	-0.111111
13			0	-1	-0.111111

Cage 4 - control (1 mouse)

Day	New weigh	Weight aft	Difference	Diff - 1ml	Amnt per mouse (ml)
0					
1		617	0	-1	-1
2	610	610	7	0	0
3	605	505	5	4	4
4	601	601	4	3	3
5	490	463	6	4	4
6	473	473	10	9	9
7			473	472	472
8			0	-1	-1
0			0	-1	-1
10			0	-1	-1
11			0	-1	-1
12			0	-1	-1
13			0	-1	-1

10015850 P9 D. McNall

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(CSF-1).pzm:Data Table- colonic disease score -

A

101.4

	Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10
1	0.0	0.0	0.0	1.0	0.0	0.0	0.0	0.0	0.0	0
2	0.0	0.0	1.0	2.0	1.0	1.0	1.0	1.0	2.0	0
3	0.0	1.0	2.0	2.0	1.0	2.0	1.0	2.0	4.0	–
4	0.0	1.0	2.0	4.0	1.0	4.0	2.0	2.0	4.0	–

Day 1 4 6 8

D. McNall 10015850 p10

(CSF-1).pzm:Data Table- colonic disease score -

B

anti-CSF-1

	Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10
1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
3	0.0	0.0	2.0	0.0	0.0	0.0	0.0	0.0	0.0	0
4	0.0	0.0	2.0	0.0	0.0	0.0	1.0	0.0	0.0	0

Day 1 4 6 8

D. McNall 10015850 p10

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(CSF-1).pzm:Data Table-clinical disease score -

A

101.4

	Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10
1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	0
2	0.0	0.0	0.0	1.0	0.0	0.0	0.0	0.0	1.0	0
3	0.0	0.0	1.0	4.0	2.0	2.0	1.0	1.0	6.0	0
4	0.0	1.0	4.0	6.0	3.0	8.0	1.0	4.0	8.0	2
5	1.0	2.0	6.0	8.0	3.0	8.0	3.0	6.0	8.0	3

Day 1 2 4 6 8

D. McNall 10015850 p11

(CSF-1).pzm:Data Table-clinical disease score -

B

anti-CSF-1

	Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10
1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
4	0.0	0.0	3.0	0.0	0.0	0.0	0.0	0.0	0.0	0
5	0.0	0.0	6.0	0.0	0.0	0.0	1.0	0.0	0.0	

Day 1 2 4 6 8

D. McNall 10015850 p11

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(CSF-1).pzm:Results-1:One-way ANOVA colon length:Tabular results -

	X Labels	A	B	C
	Parameter	Value	Data Set-B	Data Set-C
	X	Y	Y	Y
1	Table Analyzed			
2	Data Table-colon length			
3	One-way analysis of variance			
4	P value	P<0.0001		
5	P value summary	***		
6	Are means signif. different? (P < 0.05)	Yes		
7	Number of groups	3		
8	F	37.01		
9	R squared	0.7327		
10				
11	Bartlett's test for equal variances			
12	Bartlett's statistic (corrected)	7.186		
13	P value	0.0275		
14	P value summary	*		
15	Do the variances differ signif. (P < 0.05)	Yes		
16				
17	ANOVA Table	SS	df	MS
18	Treatment (between columns)	55.71	2	27.86
19	Residual (within columns)	20.32	27	0.7527
20	Total	76.04	29	
21				
22	Bonferroni's Multiple Comparison Test	Mean Diff.	t	P value
23	101.4 vs anti-CSF-1	-1.990	5.052	P < 0.001
24	101.4 vs normal control	-3.320	8.557	P < 0.001
25	anti-CSF-1 vs normal control	-1.360	3.505	P < 0.01

D. McNeill

1001555TTL

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(CSF-1).pzm:Results-3:One-way ANOVA d4 weights:Tabular results -

	X Labels	A	B	C	D
	Parameter	Value	Data Set-B	Data Set-C	Data Set-D
	X	Y	Y	Y	Y
1	Table Analyzed				
2	Data Table-6,weights table for stats				
3	One-way analysis of variance				
4	P value	0.0074			
5	P value summary	**			
6	Are means signif. different? (P < 0.05)	Yes			
7	Number of groups	3			
8	F	5.906			
9	R squared	0.3044			
10					
11	Bartlett's test for equal variances				
12	Bartlett's statistic (corrected)	1.710			
13	P value	0.4254			
14	P value summary	ns			
15	Do the variances differ signif. (P < 0.05)	No			
16					
17	ANOVA Table	SS	df	MS	
18	Treatment (between columns)	52.42	2	26.21	
19	Residual (within columns)	119.8	27	4.438	
20	Total	172.2	29		
21					
22	Bonferroni's Multiple Comparison Test	Mean Diff.	t	P value	95% CI of diff
23	control,d4 vs csf,d4	1.144	1.214	P > 0.05	-1.261 to 3.548
24	control,d4 vs 101,d4	3.195	3.392	P < 0.01	0.7906 to 5.599
25	csf,d4 vs 101,d4	2.052	2.178	P > 0.05	-0.3527 to 4.456

D. McNeill

1001555TTL

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(CSF-1).gpmcResults-1.One-way ANOVA.d5 weightsTabular results -

	X Labels Parameter	A Value	B Data Set-B	C Data Set-C	D Data Set-D
	X	Y	Y	Y	Y
1	Table Analyzed				
2	Data Table-6,weights table for stats				
3	One-way analysis of variance				
4	P value	0.0026			
5	P value summary	**			
6	Are means signif. different? (P < 0.05)	Yes			
7	Number of groups	3			
8	F	7.354			
9	R squared	0.3530			
10					
11	Bartlett's test for equal variances				
12	Bartlett's statistic (corrected)	4.783			
13	P value	0.0915			
14	P value summary	ns			
15	Do the variances differ signif. (P < 0.05)	No			
16					
17	ANOVA Table	SS	df	MS	
18	Treatment (between columns)	104.5	2	52.25	
19	Residual (within columns)	191.5	27	7.095	
20	Total	296.0	29		
21					
22	Bonferroni's Multiple Comparison Test	Mean Diff.	t	P value	95% CI of diff
23	control,d5 vs csf,d5	1.262	1.059	P > 0.05	-1.779 to 4.302
24	control,d5 vs 101,d5	4.436	3.724	P < 0.01	1.395 to 7.477
25	csf,d5 vs 101,d5	3.174	2.665	P < 0.05	0.1340 to 6.215

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(CSF-1).gpmcResults-3.One-way ANOVA (and nonparametric).Tabular results -

	X Labels Parameter	A Value	B Data Set-B	C Data Set-C	D Data Set-D
	X	Y	Y	Y	Y
1	Table Analyzed				
2	Data Table-8,weights table for stats				
3	One-way analysis of variance				
4	P value	P<0.0001			
5	P value summary	***			
6	Are means signif. different? (P < 0.05)	Yes			
7	Number of groups	3			
8	F	14.00			
9	R squared	0.5091			
10					
11	Bartlett's test for equal variances				
12	Bartlett's statistic (corrected)	9.656			
13	P value	0.0080			
14	P value summary	**			
15	Do the variances differ signif. (P < 0.05)	Yes			
16					
17	ANOVA Table	SS	df	MS	
18	Treatment (between columns)	451.5	2	225.8	
19	Residual (within columns)	435.4	27	16.13	
20	Total	886.9	29		
21					
22	Bonferroni's Multiple Comparison Test	Mean Diff.	t	P value	95% CI of diff
23	control,d8 vs csf,d8	2.160	1.203	P > 0.05	-2.424 to 8.743
24	control,d8 vs 101,d8	9.034	5.064	P < 0.001	4.510 to 13.56
25	csf,d8 vs 101,d8	6.934	3.861	P < 0.01	2.351 to 11.52

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(CSF-1).psm:Results-6:One-way ANOVA (and nonparametric):Tabular results -

	X Labels Parameter X	A Value Y	B Data Set-B Y	C Data Set-C Y	D Data Set-D Y
1	Table Analyzed				
2	Data Table-6,weights table for stats				
3	One-way analysis of variance				
4	P value	P<0.0001			
5	P value summary	***			
6	Are means signif. different? (P < 0.05)	Yes			
7	Number of groups	3			
8	F	25.98			
9	R squared	0.6581			
10					
11	Bartlett's test for equal variances				
12	Bartlett's statistic (corrected)	13.91			
13	P value	0.0010			
14	P value summary	**			
15	Do the variances differ signif. (P < 0.05)	Yes			
16					
17	ANOVA Table	SS	df	MS	
18	Treatment (between columns)	1319	2	659.6	
19	Residual (within columns)	685.4	27	25.39	
20	Total	2005	29		
21					
22	Bonferroni's Multiple Comparison Test	Mean Diff.	t	P value	95% CI of diff
23	control,d7 vs csf,d7	4.164	1.848	P > 0.05	-1.589 to 9.916
24	control,d7 vs 101,d7	15.68	6.958	P < 0.001	9.928 to 21.43
25	csf,d7 vs 101,d7	11.52	5.110	P < 0.001	5.764 to 17.27

D. McAuley 100/5856/16

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(CSF-1).psm:Results-7:One-way ANOVA (and nonparametric):Tabular results -

	X Labels Parameter X	A Value Y	B Data Set-B Y	C Data Set-C Y	D Data Set-D Y
1	Table Analyzed				
2	Data Table-5,weights table for stats				
3	One-way analysis of variance				
4	P value	P<0.0001			
5	P value summary	***			
6	Are means signif. different? (P < 0.05)	Yes			
7	Number of groups	3			
8	F	22.18			
9	R squared	0.6216			
10					
11	Bartlett's test for equal variances				
12	Bartlett's statistic (corrected)	6.456			
13	P value	0.0397			
14	P value summary	*			
15	Do the variances differ signif. (P < 0.05)	Yes			
16					
17	ANOVA Table	SS	df	MS	
18	Treatment (between columns)	2144	2	1072	
19	Residual (within columns)	1305	27	48.34	
20	Total	3448	29		
21					
22	Bonferroni's Multiple Comparison Test	Mean Diff.	t	P value	95% CI of diff
23	control,d8 vs csf,d8	5.065	1.629	P > 0.05	-2.871 to 13.00
24	control,d8 vs 101,d8	19.92	6.407	P < 0.001	11.99 to 27.88
25	csf,d8 vs 101,d8	14.86	4.778	P < 0.001	6.920 to 22.79

D. McAuley 100/5856/17

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(CSF-1).pzm:Results-11t tests (and nonparametric tests):Tabular results -

	X Labels	A
	Parameter	Value
	X	Y
1	Table Analyzed	Data Table-colonic disease score for stats
2		
3	Mann Whitney test	
4	P value	0.0021
5	Exact or approximate P value?	Gaussian Approximation
6	P value summary	**
7	Are medians signif. different? (P < 0.05)	Yes
8	One- or two-tailed P value?	Two-tailed
9	Sum of ranks in column C,G	143.5 , 66.50
10	Mann-Whitney U	11.50

d7 colonic disease score

D. MacAskill 10015850/18

(CSF-1).pzm:Results-12t tests (and nonparametric tests):Tabular results -

	X Labels	A
	Parameter	Value
	X	Y
1	Table Analyzed	Data Table-colonic disease score for stats
2		
3	Mann Whitney test	
4	P value	0.0029
5	Exact or approximate P value?	Gaussian Approximation
6	P value summary	**
7	Are medians signif. different? (P < 0.05)	Yes
8	One- or two-tailed P value?	Two-tailed
9	Sum of ranks in column D,H	143 , 67
10	Mann-Whitney U	12.00

d8 colonic disease score

D. MacAskill 10015850/18

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(CSF-1).pzm:Results-14t tests (and nonparametric tests):Tabular results -

	X Labels	A
	Parameter	Value
	X	Y
1	Table Analyzed	Data Table-clinical disease score for stats
2		
3	Mann Whitney test	
4	P value	0.0011
5	Exact or approximate P value?	Gaussian Approximation
6	P value summary	**
7	Are medians signif. different? (P < 0.05)	Yes
8	One- or two-tailed P value?	Two-tailed
9	Sum of ranks in column D,I	146 , 64
10	Mann-Whitney U	9.000

d7 clinical disease score

D. MacAskill 10015850/19

(CSF-1).pzm:Results-15t tests (and nonparametric tests):Tabular results -

	X Labels	A
	Parameter	Value
	X	Y
1	Table Analyzed	Data Table-clinical disease score for stats
2		
3	Mann Whitney test	
4	P value	0.0003
5	Exact or approximate P value?	Gaussian Approximation
6	P value summary	***
7	Are medians signif. different? (P < 0.05)	Yes
8	One- or two-tailed P value?	Two-tailed
9	Sum of ranks in column E,J	146.5 , 61.50
10	Mann-Whitney U	6.500

d8 clinical disease score

D. MacAskill 10015850/19

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(CSF-1) FACS.pzm:Results-1:One-way ANOVA (and nonparametric):Tabular results -

	X Labels / Parameter	A / Value	B / Data Set-B	C / Data Set-C	D / Data Set-D
	X	Y	Y	Y	Y
1	Table Analyzed				
2	Data Table-1, neutrophils				
3	One-way analysis of variance				
4	P value	0.0135			
5	P value summary	*			
6	Are means signif. different? (P < 0.05)	Yes			
7	Number of groups	3			
8	F	5.006			
9	R squared	0.2726			
10					
11	Bartlett's test for equal variances				
12	Bartlett's statistic (corrected)	39.54			
13	P value	P<0.0001			
14	P value summary	***			
15	Do the variances differ signif. (P < 0.05)	Yes			
16					
17	ANOVA Table	SS	df	MS	
18	Treatment (between columns)	21010000	2	10810000	
19	Residual (within columns)	55990000	27	2074000	
20	Total	77010000	29		
21					
22	Bonferroni's Multiple Comparison Test	Mean Diff.	t	P value	95% CI of diff
23	101.4 vs anti-CSF-1	1403	2.179	P > 0.05	-240.6 to 3047
24	101.4 vs normal control	1998	3.099	P < 0.05	351.9 to 3646
25	anti-CSF-1 vs normal control	592.5	0.9200	P > 0.05	-1051 to 2236

D. Thomas 5 1001585[28]

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(CSF-1) FACS.pzm:Results-3:One-way ANOVA (and nonparametric):Tabular results -

	X Labels / Parameter	A / Value	B / Data Set-B	C / Data Set-C	D / Data Set-D
	X	Y	Y	Y	Y
1	Table Analyzed				
2	Data Table-2, CD3				
3	One-way analysis of variance				
4	P value	0.0287			
5	P value summary	*			
6	Are means signif. different? (P < 0.05)	Yes			
7	Number of groups	3			
8	F	4.060			
9	R squared	0.2312			
10					
11	Bartlett's test for equal variances				
12	Bartlett's statistic (corrected)	21.97			
13	P value	P<0.0001			
14	P value summary	***			
15	Do the variances differ signif. (P < 0.05)	Yes			
16					
17	ANOVA Table	SS	df	MS	
18	Treatment (between columns)	392600000	2	196300000	
19	Residual (within columns)	1305000000	27	48330000	
20	Total	1697000000	29		
21					
22	Bonferroni's Multiple Comparison Test	Mean Diff.	t	P value	95% CI of diff
23	101.4 vs anti-CSF-1	6837	2.169	P > 0.05	-1101 to 14770
24	101.4 vs normal control	9301	2.869	P < 0.05	353.3 to 16249
25	anti-CSF-1 vs normal control	1464	0.4707	P > 0.05	-5474 to 8401

D. Thomas 1001585[27]

ASSESSED AND UNDERSTOOD DATE ..../..../.... INVENTED BY ..... DATE ..../..../....

BY ..../..../.... RECORDED BY D. Thomas DATE .....

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TITLE: anti-CSF-1

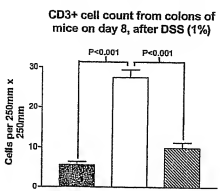
PAGE No. 22

DATE

PROJECT NO

NOTEBOOK NO 10015850

CD3+ cell counts by immunohistochemistry from James Cameron.



n = 10. Antibodies injected weekly at 10mg/kg sub cut.
1st injection 24hrs before addition of 1% DSS to drinking water
Statistical analysis by ANOVA with Bonferroni's post test.

10015850/22

ASSESSED AND UNDERSTOOD DATE INVENTED BY ..... DATE...../...../.....

BY..... ...../...../..... RECORDED BY D Thrussell DATE.....

TITLE: anti-CSF-1

PAGE No. 23

DATE

PROJECT NO

NOTEBOOK NO 10015850

CD3+ cell counts by immunohistochemistry from James Cameron

Block No.	Animal No.	Counts										
887-03	101.4 gp 1,1	22	23	28	22	38	27	24	18	32	22	25.4
888-03	101.4 gp 1,2	22	18	27	28	23	20	19	28	27	28	23.6
889-03	101.4 gp 1,3	41	64	40	42	26	30	30	20	23	51	35.7
890-03	101.4 gp 1,4	17	21	16	14	31	15	19	32	33	18	21.6
891-03	101.4 gp 1,5	18	28	21	13	20	18	28	21	19	32	21.4
892-03	101.4 gp 1,6	38	31	34	23	37	22	23	36	30	22	30.4
893-03	101.4 gp 1,7	39	38	43	20	24	32	14	18	23	30	30.9
894-03	101.4 gp 1,8	14	20	38	30	38	81	24	16	24	22	28.5
895-03	101.4 gp 1,9	31	30	12	8	8	14	16	28	20	35	19.9
896-03	101.4 gp 1,10	48	39	27	35	52	42	35	25	35	33	37
897-03	ab 33 gp 2,1	6	9	11	17	9	5	3	4	4	0	7.2
898-03	ab 33 gp 2,2	6	8	13	17	12	6	5	5	9	9	9.2
899-03	ab 33 gp 2,3	19	15	19	15	16	15	13	13	10	20	15.4
900-03	ab 33 gp 2,4	15	9	14	6	24	12	13	12	18	8	13.1
901-03	ab 33 gp 2,5	1	8	3	4	9	1	3	7	7	7	4.7
902-03	ab 33 gp 2,6	8	11	10	8	7	11	6	7	5	5	7.9
903-03	ab 33 gp 2,7	16	21	20	25	12	22	10	12	9	23	17.2
904-03	ab 33 gp 2,8	10	13	9	4	6	6	14	10	11	11	9.4
905-03	ab 33 gp 2,9	12	9	10	10	13	11	14	8	10	8	10.5
906-03	ab 33 gp 2,10	2	3	2	11	3	7	6	9	4	3	4.9
907-03	normal gp3,1	7	9	4	3	4	6	4	5	6	3	5.3
908-03	normal gp3,2	3	5	5	2	4	3	2	4	4	3	3.6
909-03	normal gp3,3	6	10	6	5	6	3	2	7	3	6	5.4
910-03	normal gp3,4	4	7	5	6	4	4	5	8	5	3	5
911-03	normal gp3,5	3	3	5	4	3	6	5	6	7	4	4.3
912-03	normal gp3,6	1	2	4	1	2	4	7	6	3	5	3.4
913-03	normal gp3,7	12	12	10	10	4	7	7	8	9	7	8.6
914-03	normal gp3,8	1	7	3	3	6	4	3	1	2	6	3.6
915-03	normal gp3,9	5	4	4	2	5	6	8	7	4	12	5.6
916-03	normal gp3,10	15	10	8	14	13	20	9	8	9	9	11.6

D Thrussell 10015850/23

ASSESSED AND UNDERSTOOD DATE INVENTED BY ..... DATE...../...../.....

BY..... ...../...../..... RECORDED BY D Thrussell DATE.....

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TITLE: anti-CSF-1

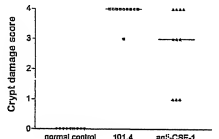
PAGE No.

DATE

PROJECT NO

NOTEBOOK NO 101.1550

Histological crypt damage score from colons of mice on day 8 after administration of DSS



By ANOVA anti-CF1 treatment led to less histological crypt damage than mice with DSS colitis and treatment with 101.4

D. Thomas

101.1550/24

Block No.	Animal No.	Damage
887 -03	101.4 gp 1,1	3
888 -03	101.4 gp 1,2	4
889 -03	101.4 gp 1,3	4
890 -03	101.4 gp 1,4	4
891 -03	101.4 gp 1,5	4
892 -03	101.4 gp 1,6	4
893 -03	101.4 gp 1,7	4
894 -03	101.4 gp 1,8	4
895 -03	101.4 gp 1,9	4
896 -03	101.4 gp 1,10	4
897 -03	ab 33 gp 2,1	3
898 -03	ab 33 gp 2,2	1
899 -03	ab 33 gp 2,3	4
900 -03	ab 33 gp 2,4	3
901 -03	ab 33 gp 2,5	4
902 -03	ab 33 gp 2,6	1
903 -03	ab 33 gp 2,7	4
904 -03	ab 33 gp 2,8	4
905 -03	ab 33 gp 2,9	3
906 -03	ab 33 gp 2,10	1
907 -03	normal gp3,1	0
908 -03	normal gp3,2	0
909 -03	normal gp3,3	0
910 -03	normal gp3,4	0
911 -03	normal gp3,5	0
912 -03	normal gp3,6	0
913 -03	normal gp3,7	0
914 -03	normal gp3,8	0
915 -03	normal gp3,9	0
916 -03	normal gp3,10	0

D. Thomas

101.1550/24

ASSESSED AND UNDERSTOOD DATE INVENTED BY ..... DATE...../...../.....

BY..... ...../...../..... RECORDED BY D. Thomas DATE.....

TITLE: anti-CSF-1

PAGE No. 25

DATE

PROJECT NO

NOTEBOOK NO 101.1550

CSF-1) damage score.pzmResults-3:One-way ANOVA (and nonparametric)Tabular results -

	X Labels	A	B	C	D
	Parameter	Value	Data Set-B	Data Set-C	Data Set-D
	X	Y	Y	Y	Y
1	Table Analyzed				
2	Data Table-1				
3	One-way analysis of variance				
4	P value	P<0.0001			
5	P value summary	***			
6	Are means signif. different? (P < 0.05)	Yes			
7	Number of groups	3			
8	F	68.16			
9	R squared	0.8306			
10					
11	Bartlett's test for equal variances				
12	Bartlett's statistic (corrected)				
13	P value				
14	P value summary	ns			
15	Do the variances differ signif. (P < 0.05)	No			
16					
17	ANOVA Table	SS	df	MS	
18	Treatment (between columns)	80.67	2	40.43	
19	Residual (within columns)	16.50	27	0.6111	
20	Total	97.37	29		
21					
22	Bonferroni's Multiple Comparison Test	Mean Diff.	t	P value	95% CI of diff
23	101.4 vs anti-CSF-1	1.100	3.148	P < 0.05	0.2077 to 1.992
24	101.4 vs normal control	3.900	11.16	P < 0.001	3.008 to 4.792
25	anti-CSF-1 vs normal control	2.800	8.009	P < 0.001	1.908 to 3.692

101.1550 & 24/25

D. Thomas

ASSESSED AND UNDERSTOOD DATE INVENTED BY ..... DATE...../...../.....

BY..... ...../...../..... RECORDED BY D. Thomas DATE.....

TITLE: anti-CSF-1

PAGE No. 4

DATE

PROJECT NO

NOTEBOOK NO 1661/5850

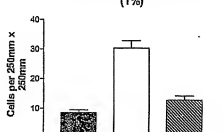
F4/80+ cell count from colons of mice on day 8, after DSS (1%)

D McGrath

1661/5850/26

by ANOVA with Bonferroni post test anti-CSF-1 treated mice had fewer F4/80+ cells than 101.4 treated mice $P < 0.001$

F4/80+ cell count from colons of mice on day 8, after DSS (1%)



D McGrath

1661/5850/26

ASSESSED AND UNDERSTOOD	DATE	INVENTED BY	DATE
BY	../../..	RECORDED BY D McGrath	DATE

TITLE: anti-CSF-1

PAGE No. 27

DATE

PROJECT NO

NOTEBOOK NO 1661/5850

F4/80+ cell count

Block No.	Animal No.	Counts									
897-03	101.4 gp 1,1	16	22	25	21	24	12	20	25	14	14	19.3
898-03	101.4 gp 1,2	21	32	29	24	25	17	19	28	19	25	23.6
899-03	101.4 gp 1,3	27	49	39	50	47	29	21	29	42	39	39.7
900-03	101.4 gp 1,4	14	18	27	31	25	16	43	17	18	24	23.1
901-03	101.4 gp 1,5	28	40	30	35	31	24	16	17	20	34	27.6
902-03	101.4 gp 1,6	37	48	76	53	53	34	31	30	34	34	43.9
903-03	101.4 gp 1,7	29	37	35	30	25	30	23	30	42	35	31.6
904-03	101.4 gp 1,8	38	29	48	53	46	41	38	21			39
905-03	101.4 gp 1,9	29	31	20	20	25	29	30	38			28.25
906-03	101.4 gp 1,10	29	32	35	32	28	44	41	31	32	25	31.6
907-03	ab 33 gp 2,1	10	13	18	18	8	10	9	7	14	8	10.9
908-03	ab 33 gp 2,2	7	8	4	9	12	3	8	3	4	8	8.2
909-03	ab 33 gp 2,3	10	36	13	11	17	10	20	21	13	20	17.9
900-03	ab 33 gp 2,4	10	15	11	13	8	29	22	12	17	18	16.2
901-03	ab 33 gp 2,5	12	9	9	8	9	27	28	14	17	18	14.6
902-03	ab 33 gp 2,6	5	10	20	20	12	12	19	11	9	10	12.8
903-03	ab 33 gp 2,7	15	16	10	14	8	28	23	33	13	14	17.5
904-03	ab 33 gp 2,8	7	9	12	11	13	10	14	8	8	10	10
905-03	ab 33 gp 2,9	20	13	23	17	20	17	17	25	11	19	19.2
918-03	ab 33 gp 2,10	9	9	4	5	4	4	4	9	8	6	5.8
907-03	normal gp0,1	10	8	16	6	5	8	8	14	11	9	9.2
908-03	normal gp0,2	13	12	18	15	19	14	11	16	16	16	14.9
909-03	normal gp0,3	6	8	10	10	10	11	6	9	9	8	8.8
910-03	normal gp0,4	14	7	10	8	12	13	8	19	10	11	11.2
911-03	normal gp0,5	5	4	3	11	14	9	3	8	9	9	7.3
912-03	normal gp0,6	5	6	3	1	1	2	5	8	8	5	4.5
913-03	normal gp0,7	12	9	9	7	14	9	7	7	7	12	9.2
914-03	normal gp0,8	5	3	7	8	4	8	12	7	5	4	6.2
915-03	normal gp0,9	4	9	2	5	11	12	2	1	6	3	5.5
916-03	normal gp0,10	6	10	5	11	13	10	8	6	8	8	8.5

D McGrath

1661/5850/24

ASSESSED AND UNDERSTOOD	DATE	INVENTED BY	DATE
BY	../../..	RECORDED BY D McGrath	DATE

TITLE: anti - CSF-1

PAGE No. 2

DATE
PROJECT NO
NOTEBOOK NO ...10015850

(CSF-1) f480.pzm:Results-1:One-way ANOVA (and nonparametric):Tabular results -

	X Labels	A	B	C	D
	Parameter	Value	Data Set-B	Data Set-C	Data Set-D
	X	Y	Y	Y	Y
1	Table Analyzed				
2	Data Table-1				
3	One-way analysis of variance				
4	P value	P<0.0001			
5	P value summary	***			
6	Are means signif. different? (P < 0.05)	Yes			
7	Number of groups	3			
8	F	45.14			
9	R squared	0.7698			
10					
11	Bartlett's test for equal variances				
12	Bartlett's statistic (corrected)	7.422			
13	P value	0.0244			
14	P value summary	*			
15	Do the variances differ signif. (P < 0.05)	Yes			
16					
17	ANOVA Table	SS	df	MS	
18	Treatment (between columns)	2688	2	1343	
19	Residual (within columns)	803.4	27	29.76	
20	Total	3490	29		
21					
22	Bonferroni's Multiple Comparison Test	Mean Diff.	t	P value	95% CI of diff
23	101.4 vs anti-CSF-1	17.56	7.198	P < 0.001	11.33 to 23.78
24	101.4 vs normal control	21.89	8.971	P < 0.001	15.66 to 28.11
25	anti-CSF-1 vs normal control	4.330	1.775	P > 0.05	-1.897 to 10.56

D McNaull, 10015850128

ASSESSED AND UNDERSTOOD BY ....../....../...... DATE

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RECORDED BY D. McNaull DATE

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TITLE: anti - CSF-1

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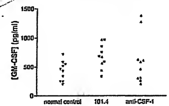
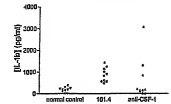
PROJECT NO
NOTEBOOK NO :10015850

D. McNaull

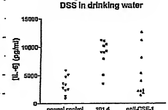
GM-CSF concentrations in mouse colon culture supernatants following administration of 1% DSS in drinking water



IL-1b concentrations in mouse colon culture supernatants following administration of 1% DSS in drinking water

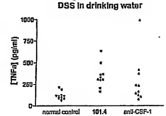


IL-6 concentrations in mouse colon culture supernatants following administration of 1% DSS in drinking water



10015850129

TNFa concentrations in mouse colon culture supernatants following administration of 1% DSS in drinking water



The anti-CSF-1 antibody is tending to decrease cytokine release into supernatant, but this is not statistically significant.

ASSESSED AND UNDERSTOOD	DATE	INVENTED BY	DATE....../....../......
BY	....../....../......	RECORDED BY D. McNaull	DATE

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TITLE: anti-CSF-1

DATE

PROJECT NO

NOTEBOOK NO 10015850

CALCULATED CONCENTRATION

GM-CSF

BACKGROUND VALUE 27

	1	2	3	4	5	6	7	8	9	10	11	12
A		459.73	278.22	169.81	84.727	8.97	590.78	858.37	627.73	200.62		
B		316.19	303.08	175.93	50.575	25.491	565.11	303.59	587.24	481.73		
C		34.727	194.48	183.94	31.153	8.97	338.59	312.19	810.41	515.83		
D		194.48	151.81	75.578	55.883	8	971.08	1379	340.96	430.5		
E		263.54	329.45	93.204	44.815	8	963.97	281.29	587.24	248.35		
F		166.89	206.62	87.212	8.97	0	688.6	199.94	250.43			
G		567.63	271.3	140.85	8	0	758.33	457.74	548.08			
H		261.85	238.05	52.388	0	435.03	670.55	1276	720.62			

IL-1beta

BACKGROUND VALUE 2

	1	2	3	4	5	6	7	8	9	10	11	12
A		720.43	645.36	185.47	645.36	809.68	1443.6	1238.7	858.53	185.47		
B		466.83	185.47	217.86	639.26	923.26	1144.1	217.86	185.47	97.785		
C		527.18	185.47	124.6	541.38	868.02	568.87	8	0	246.63		
D		601.73	124.6	1121.4	608.12	814.47	1018	1314.4	296.95	8		
E		648.94	147.26	1009.7	620.75	1005.5	614.47	147.26	217.86	380.47		
F		1440.5	340.87	512.66	814.68	768.75	819.65	147.26	185.47			
G		555.26	0	1129	1270.1	620.75	909.71	97.705	0			
H		1300.9	97.705	534.32	779.16	462.51	555.26	3089	147.26			

IL-6

BACKGROUND VALUE 5

	1	2	3	4	5	6	7	8	9	10	11	12
A		6674	3623	2040.5	288.14	288.14	9052	10200	8128.7	682.91		
B		3760.4	1552.7	855.45	241.97	276.21	9084.1	2378.8	5419.9	3564.1		
C		1042.9	2215.8	1877.9	186.43	295.85	5075.5	2241.7	2225	4745.5		
D		2566.8	1790	8	241.97	255.27	11100	12600	2367.8	3360.5		
E		3300.8	1569.1	641.13	288.14	325.13	10500	1893.1	2518.7	2778.9		
F		2020.3	721.47	568.81	272.14	263.83	11200	1442.3	1343.6			
G		8121.9	1950.8	358.8	368.37	272.14	9310.2	4034.2	5109			
H		6398.4	732.09	208.11	292.02	3475.8	7933.4	11200	5930.8			

TNF-alpha

BACKGROUND VALUE 24

	1	2	3	4	5	6	7	8	9	10	11	12
A		288.18	212.25	79.427	184.38	103.91	329.58	368.73	233.34	81.908		
B		118.98	81.908	49.284	148.07	109.76	633.99	239.38	372.26	117.18		
C		107.84	81.908	65.858	135.70	124.22	165.04	105.89	124.22	124.22		
D		254.89	49.284	137.36	179.39	84.328	299.14	417.41	214.43	[illegible]		
E		113.52	81.908	282.98	129.29	117.18	360.15	186.38	86.687	[illegible]		
F		169.05	65.856	187.56	138.95	95.626	304.92	146.59	62.845			
G		252.99	86.687	219.82	171.69	103.91	495.74	76.878	113.52			
H		233.34	52.955	155.33	117.18	204.44	309	988.04	113.52			

1,1 → 1,10 H6 → A8
2,1 → 2,10 B8 → C9
3,1 → 3,10 D9 → E10

10015850/30
D. McDaull

Luminex performed by BC. using R+D reagents.

ASSESSED AND UNDERSTOOD BY REDACTED DATE ../../..

INVENTED BY .... DATE ../../..

RECORDED BY D. McDaull DATE

TITLE: Anti-CSF-1 in DSS-colitis in mice

DATE

PROJECT NO

NOTEBOOK NO 160158So

DSS model of IBD (mice).

Aim
To assess the effects of anti-CSF-1 antibody on DSS induced colitis in mice.

Procedure
Licence 70/5748, procedure 19
Balb/c mice (males, batch RM3326, arrived [redacted] 18-22g) weighed and injected subcutaneously with mAb @ 10mg/kg.
Group 1 – 101.4, control antibody (lot- 1001442G/15) – (γ1 isotype)
Group 2 – Anti-CSF-1, alkylated A823 (4.7mg/kg ⇒)
10 mice in each group. Normal drinking water then replaced with 1% DSS (ICN MW 36-50K, Cat No 160110) in tap water 24 hours after 1st antibody injection. Lot n° 4347F

Group 3 – No treatment control group
10 mice will continue to have normal drinking water.

Mice will receive antibody once a week. Animals will be weighed each day and signs of disease (loose stools, bleeding) noted. The volume of 1% DSS or water consumed also measured by weight. At end of expt., colons will be removed and length measured. A 1 cm section will be collected from the distal end for assessment of neutrophil and T cell infiltration by FACS analysis. The next 2 cm section will be collected and placed in formalin for histological analysis. The next cm will be place in culture medium for 24 hours, after which time the supernatant will be collected and cytokine levels measured by luminex. Plasma will also be collected at termination.

D. Mc Brow
Study Period

160158So/53

This experiment is an exact repeat of the experiment on p of this book.
Disease incidence was low in this expt, however the anti-CSF-1 antibody does seem to again protect from weight loss, although there was no significant difference between the 101.4 vs anti-CSF-1 groups until day 10

ASSESSED AND UNDERSTOOD | DATE | INVENTED BY ..... | DATE...../...../.....
BY..... | ...../...../..... | RECORDED BY ..... | DATE...../...../.....

TITLE: Anti-CSF-1 in DSS-colitis in mice (2)

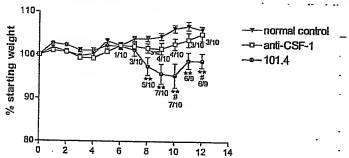
PAGE No. 54

DATE

PROJECT NO

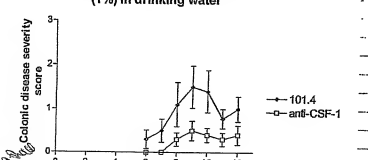
NOTEBOOK NO 1001S850

Effect of anti-CSF-1 Ab on body weight of mice after addition of DSS (1%) in drinking water



Antibodies injected weekly at 10mg/kg sub cut.,
1st injection 24hrs before addition of 1% DSS to drinking water
Statistical analysis by ANOVA with Bonferroni's post test:-
** P<0.01 101.4 vs normal animals, # P<0.05 101.4 vs anti-CSF-1
No significant difference between anti-CSF-1 and normal animals

Effect of anti-CSF-1 Ab on colonic disease severity score of mice after addition of DSS (1%) in drinking water



D.MacNeil 1001S850 P54

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TITLE: Anti-CSF-1 (2)

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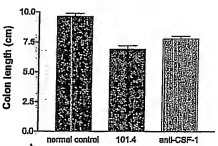
Effect of anti-CSF-1 Ab on colon length of mice after addition of DSS (1%) in drinking water for 8 days



D.MacNeil 1001S850 P55

mice (CSF-1,2).pzmDat

	A anti-CSF-1 Y	B 101.4 Y	C normal contr Y
1	7.70	7.80	10.10
2	7.90	8.20	10.10
3	7.10	7.20	8.90
4	8.00	7.40	10.00
5	6.80	8.30	9.60
6	6.80	6.80	9.70
7	8.80	7.00	10.40
8	6.80	6.90	9.20
9	6.30	6.80	8.10
10	7.80	4.80	10.70

D.MacNeil 1001S850 P55

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Cage 1 - DSS + anti-CSF-1

mouse weights

day	animal number												
	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	27.1	26	27.1	26.5	28.7	27.5	26.6	26.6	24.0	27.3	26.62	0.775743	0.245488
1	27	25.1	27.3	26.7	27.2	27.0	27	26.7	25	26.4	26.9	0.903081	0.285785
2	27.4	26.1	27	27	27.1	27.9	26.6	26.4	24.9	27.6	26.62	0.858881	0.271735
3	26.8	25.8	26.3	25.4	26.0	27.8	26.7	26.2	24.7	27.5	26.40	0.830201	0.262741
4	26.7	25.8	26.4	25.6	26.4	27.5	26.3	26.1	24.8	27.7	26.43	0.819282	0.259268
5	27.1	26.2	26.7	27.1	27.1	27.7	27.3	26.1	25.2	27.9	26.84	0.812677	0.257176
6	27.9	26.8	28.5	27.8	27.5	27.9	28.1	26.5	25.2	28.2	27.22	0.953124	0.301621
7	27.8	26.7	28.2	27.7	27.7	27.7	28.4	26.3	24.9	28.5	27.17	1.124925	0.355882
8	27.8	26.8	25.8	27.6	27.6	27.3	28.2	28	25	28.5	27.07	1.142171	0.361447
9	28.2	27	28	27.8	27.7	25.9	28.3	25.8	25.1	28.7	27.03	1.252597	0.396392
10	28.3	27.1	26.8	28.1	27.9	27.1	28.1	25.1	25.4	29.3	27.32	1.308774	0.414169
11	28.7	27.8	27.1	28.2	28.4	27.2	28.9	24.5	25.7	29.6	27.59	1.546645	0.489445
12	28.1	27.6	27.3	28.4	28.7	28.2	29.4	24.9	26.3	28.8	27.58	1.522571	0.481826

DSS + 101-4

day	animal number												
	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	26.7	27.2	24.8	24.9	26.4	26	25.4	25.5	26.5	23.5	25.69	1.099949	0.348085
1	27.3	27.0	25.7	26.2	27.5	28.5	25.6	25.8	27.4	23.0	26.38	1.201608	0.380274
2	27.2	27.8	25.4	26.1	27.4	26.4	26	25.0	27.2	23.9	26.28	1.140955	0.361062
3	27.1	27.2	26.4	26.7	27.3	26	25.8	25.2	26.7	23.4	25.98	1.18865	0.378155
4	27.1	27.1	25.5	25.7	27	26.2	26.9	24.8	26.8	23.5	25.97	1.149528	0.363901
5	27.5	27.8	25.8	26.3	27.4	26.7	25.7	25.2	26.9	23.5	26.28	1.269471	0.401731
6	27.2	27.7	25.7	25.9	27.6	27	25.8	25.4	27	22.9	26.22	1.434341	0.453909
7	27.2	27	26.3	26.1	28	26.6	25.8	24.9	27	21.3	26.04	1.870947	0.592072
8	26.6	25.4	25.3	25.3	27.2	26.3	25.2	23.7	26.5	19.2	25.07	2.285243	0.723178
9	23.5	24.5	25.3	25.1	27.4	25.5	24.5	23.4	25.7	18.4	24.63	2.451779	0.77589
10	26.4	24	25.8	25.5	27.8	25.4	24.3	23.5	25.3	17.3	24.53	2.776108	0.878515
11	26.7	24	25.8	25.5	20	26	24.7	24.4	25		25.61111	1.246439	0.394443
12	25.7	24.9	25.9	25.8	27.4	26	24.9	24.4	24.8		25.6	1.031988	0.326579

control

day	animal number												
	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	20.3	26.7	24.7	24.7	26.6	26.6	25.9	25	27.2	25.8	25.33	1.977681	0.625848
1	20.9	27.1	28	25.2	20.5	27.2	26.6	26.3	27.2	26.5	25.75	1.899269	0.601034
2	21	27.1	24.8	24.8	26.0	26.2	26.5	24.9	27.1	26.3	25.53	1.826969	0.578161
3	20.2	26.5	24.5	24.8	26.4	26.5	25.8	25	26.9	26.1	25.27	1.958488	0.619774
4	20.5	26.9	25.1	24.8	26.4	26.5	26.0	24.8	27	26.3	25.39	1.90501	0.603104
5	21.4	27.3	28	25.2	26.9	27.2	27	28	27.5	27	26.15	1.818577	0.575459
6	21.5	27.1	25.4	28	26.9	27.2	26.4	26.3	27.5	26.5	25.08	1.766271	0.558932
7	21.8	27.3	26.3	25.7	27.1	27.4	27.1	25.5	26.1	26.5	26.20	1.764318	0.558335
8	21.8	27.6	26.6	25.3	27.4	26.8	26.6	25.7	28.1	26.7	26.29	1.762913	0.564213
9	22.1	28	25.8	25.7	27.4	27.5	27.1	25.4	28.1	25.8	26.41	1.773913	0.561048
10	22.7	28.2	27	25.7	27.8	28.2	27.7	26.2	28	27.2	26.87	1.689873	0.53477
11	23	28.4	27.3	25.7	28	27.8	28.2	26.3	28.2	27.3	27.02	1.601191	0.525693
12	22.4	28.4	27.3	26	27.6	28	27.4	26	28	27.1	26.82	1.745343	0.552324

D.MacDall

100158 50/56

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TITLE: Anti-CSF-1 (2)

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Cage 1 -

mouse weights

day	animal number												
	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	100	100	100	100	100	100	100	100	100	100	100	0	0
1	99.831	100.3848	100.738	100.7547	101.8727	100.3636	101.5038	100.3758	100.8065	104.0203	101.848	1.219408	0.385914
2	101.197	100.3048	99.631	101.8868	101.4981	101.4545	100.7519	99.24812	100.4032	101.0989	100.7404	0.840569	0.266003
3	98.89289	99.23077	97.04797	99.82264	99.82547	100.3636	100.3759	98.49624	99.59677	100.7326	99.3985	1.076543	0.340878
4	98.62399	99.23077	97.41697	100.3774	99.8764	100	98.87218	98.1203	100	101.4652	99.28832	1.169508	0.370427
5	100	100.7692	98.62380	102.2042	101.4001	100.7273	102.6316	98.1203	101.8129	102.1978	100.8345	1.548043	0.400203
6	102.952	103.0769	97.70598	104.1509	102.9963	101.4545	105.6391	99.62400	101.8129	103.2967	102.2589	2.2558	0.713708
7	101.849	102.6923	96.67897	104.5283	103.7453	100.7273	106.7669	98.87218	100.4032	104.3958	102.0655	2.903093	0.947101
8	102.952	103.0769	95.20295	104.1509	103.3708	99.27273	106.015	97.74436	100.8065	104.3956	101.6988	3.37798	1.080901
9	104.059	103.8462	95.84096	104.1509	103.7453	94.10182	106.391	96.99248	101.2097	105.1282	101.5648	4.286045	1.359181
10	104.428	104.2308	98.89290	106.0377	104.4944	98.54545	105.6391	94.3609	102.4194	107.326	102.0375	4.096900	1.293489
11	105.0041	106.1539	100	106.4151	106.367	98.90909	108.6468	92.10526	103.629	108.4249	103.6555	5.108545	1.845130
12	107.3801	108.1538	100.738	107.1088	107.4900	102.5455	110.5263	93.23308	108.0404	109.1575	105.0443	5.049331	1.59709

day	animal number												
	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	100	100	100	100	100	100	100	100	100	100	100	0	0
1	102.2472	102.2039	103.828	105.2208	104.1607	101.9231	101.5748	101.1765	103.3002	101.2766	102.6017	1.354884	0.428598
2	101.8727	101.4706	103.4194	104.6193	103.7870	101.5385	102.3622	100.3922	102.6415	101.7021	102.3008	1.253578	0.393701
3	101.4981	100	103.4194	103.2128	103.4091	100	101.5748	98.82353	100.7647	99.57447	101.1267	1.562133	0.484346
4	101.4981	99.63235	103.8228	103.2129	102.2727	100.7692	101.9685	97.64706	101.1321	100	101.0950	1.670547	0.520554
5	102.9963	101.4706	104.0323	105.6225	103.7870	102.6923	101.1811	98.82353	101.5094	100	102.2110	2.020854	0.639511
6	101.8727	101.8382	103.829	104.0161	104.5455	103.8462	101.5748	99.60704	101.8868	97.44681	103.0284	2.193143	0.694033
7	101.8727	99.26471	106.0484	104.0193	100.0600	103.0769	101.5748	97.64706	101.8868	90.6383	101.289	4.626712	1.404149
8	99.62547	93.38235	102.0161	101.6084	103.0303	101.1538	99.2128	92.94118	100	81.70213	97.48704	8.516589	2.052212
9	99.25094	90.07353	102.0161	100.0032	103.7878	98.07692	98.45669	81.76471	98.98113	78.29787	95.7509	7.468778	2.337934
10	98.8764	88.23529	103.2258	102.4096	104.5455	97.69231	95.66929	93.72549	95.4717	73.61702	95.34684	8.007908	2.66958
11	100	88.23528	104.0323	104.0101	100.0600	100	97.24409	95.66027	94.33962		98.84802	5.032332	1.769383
12	100	90.07353	104.4355	103.6145	103.7879	100	98.0315	95.66027	93.58401		98.80158	4.853925	1.507698

day	animal number												
	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	100	100	100	100	100	100	100	100	100	100	100	0	0
1	102.9557	101.4981	101.2148	103.0243	99.62400	102.2558	102.7027	101.2	100	103.5156	101.8991	1.240039	0.374549
2	103.4403	101.4981	100.4048	100.4049	100	98.45024	102.3160	98.8	99.83235	103.7344	100.8538	1.583039	0.501268
3	99.50739	99.25094	99.19028	100.4049	99.24812	99.62406	99.6139	100	98.09706	101.9531	99.70097	0.880434	0.278618
4	100.5952	100.7491	101.6194	100.4049	99.24812	99.62406	98.8417	99.2	99.28471	102.7344	100.2672	1.200065	0.35934
5	105.4107	102.2472	105.2632	102.0243	101.1278	102.2556	104.2471	104	101.1029	105.4688	103.3158	1.757818	0.556200
6	105.9113	101.4981	102.834	101.2146	101.1278	102.2556	101.9305	101.2	101.1029	103.5156	102.2591	1.510934	0.480975
7	107.3092	102.2472	106.4777	104.0468	101.0797	103.0075	104.8332	102	103.3088	103.5158	103.8509	1.853001	0.597094
8	107.3892	109.3708	107.6923	102.4291	103.0075	101.1278	103.4749	102.8	103.3008	104.2968	103.8897	2.091718	0.661035
9	108.867	104.8685	108.502	104.0460	103.9075	103.2835	104.8332	103.2	103.3088	100	104.382	2.827582	0.831517
10	111.0227	105.818	109.3117	104.0488	104.5113	108.015	100.9498	104.8	102.9412	100.25	106.2208	2.830759	0.832519
11	113.3005	106.367	110.5263	104.0466	105.2632	104.5113	108.8893	103.2	103.6785	108.8400	106.8414	3.120045	0.890394
12	110.3448	108.367	110.5263	105.2632	103.7594	105.2632	105.7815	104	102.9412	105.6594	106.0110	2.560900	0.810474

D.MacDall

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TITLE: Anti-CSF-1 (2)

PAGE No.

DATE

PROJECT NO

NOTEBOOK NO 10015850

mice (CSF-1,2).psm:Data Table-3, disease -

	A				anti-CSF-1					
	Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10
1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
3	0.0	0.0	1.0	0.0	0.0	1.0	0.0	1.0	0.0	0
4	0.0	0.0	1.0	0.0	0.0	2.0	0.0	1.0	1.0	0
5	0.0	0.0	1.0	0.0	0.0	1.0	0.0	1.0	1.0	0
6	0.0	0.0	0.0	0.0	0.0	1.0	0.0	1.0	1.0	0
7	0.0	0.0	0.0	0.0	0.0	1.0	0.0	2.0	1.0	0

D. Mitchell

10015850/58

mice (CSF-1,2).psm:Data Table-3, disease -

	B				101.4					
	Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10
1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.0	0.0	1
2	0.0	1.0	0.0	0.0	0.0	0.0	0.0	2.0	0.0	2
3	0.0	1.0	0.0	0.0	0.0	1.0	1.0	4.0	0.0	4
4	1.0	2.0	0.0	0.0	0.0	2.0	1.0	4.0	1.0	4
5	1.0	2.0	0.0	0.0	0.0	1.0	1.0	4.0	1.0	4
6	1.0	1.0	0.0	0.0	0.0	1.0	1.0	2.0	1.0	
7	1.0	2.0	0.0	0.0	0.0	2.0	1.0	2.0	1.0	

10015850/58

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TITLE: Anti-CSF-1 (2)

PAGE No. 59

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NOTEBOOK NO 10015850

mice (CSF-1,2).psm:Results-1:One-way ANOVA (and nonparametric):Tabular results -

	X Labels	A	B	C
	Parameter	Value	Data Set-B	Data Set-C
	X	Y	Y	Y
1	Table Analyzed			
2	Data Table-2,colon length			
3	One-way analysis of variance			
4	P value	P<0.0001		
5	P value summary	***		
6	Are means signif. different? (P < 0.05)	Yes		
7	Number of groups	3		
8	F	27.42		
9	R squared	0.6733		
10				
11	Bartlett's test for equal variances			
12	Bartlett's statistic (corrected)	0.5783		
13	P value	0.7489		
14	P value summary	ns		
15	Do the variances differ signif. (P < 0.05)	No		
16				
17	ANOVA Table	SS	df	MS
18	Treatment (between columns)	36.59	2	18.30
19	Residual (within columns)	18.73	27	0.6936
20	Total	57.32	29	
21				
22	Bonferroni's Multiple Comparison Test	Mean Diff.	t	P value
23	anti-CSF-1 vs 101.4	0.8700	2.339	P > 0.05
24	anti-CSF-1 vs normal control	-1.850	4.967	P < 0.001
25	101.4 vs normal control	-2.720	7.303	P < 0.001

D. Mitchell 10015850/59

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TITLE: anti-CSF-1 — DSS colitis (3)

PAGE No. 60

DATE

PROJECT NO

NOTEBOOK NO : 10015850

- DSS model of IBD (mice).

Aim
To assess the effects of anti-CSF-1 antibody on DSS induced colitis in mice.

Procedure
Licence 70/5748, procedure 19.
Balb/c mice (males, batch RM3357, arrived [20-25g) weighed and injected subcutaneously with mAb @ 10mg/kg.
Group 1 – 101.4, control antibody (lot:- 10014426/15) – (γ1 isotype) twice a week
Group 2 – 101.4, control antibody (lot:- 10014426/15) – (γ1 isotype) once a week
Group 4 – Anti-CSF-1, alkylated Ab33 (4.7mg/ml) twice a week
Group 5 – Anti-CSF-1, alkylated Ab33 (4.7mg/ml) once a week lot 4379F

10 mice in each group. Normal drinking water then replaced with 1% DSS (ICN MW 36-50K, Cat No 160110) in tap water 24 hours after 1st antibody injection.

Group 3 – No treatment control group
10 mice will continue to have normal drinking water.

Mice will receive antibody once a week. Animals will be weighed each day and signs of disease (loose stools, bleeding) noted. The volume of 1% DSS or water consumed also measured by weight. At end of expt., colons will be removed and length measured. A 1 cm section will be collected from the distal end for assessment of neutrophil and T cell infiltration by FACS analysis. The next 2 cm section will be collected and placed in formalin for histological analysis. Plasma will also be collected at termination.

Study Period

D. McDall 10015850/60

Very severe disease was noted in this experiment, which the anti-CSF-1 failed to inhibit. Therefore it appears that the anti-CSF-1 can inhibit mild disease in DSS administered mice, but not severe disease.
Will carry out next experiment with the Pegylated-Fab of Ab33.

Raw data in file 10017550

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TITLE: anti-CSF-1 (3)

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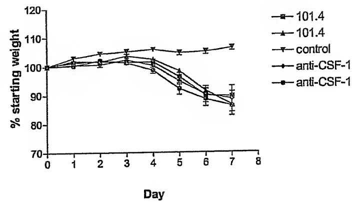
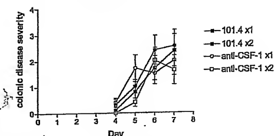
Effect of anti-CSF-1 Ab on colon length of mice after addition of DSS (1%) in drinking water for 7 days



Effect of anti-CSF-1 Ab on colonic disease of mice after addition of DSS (1%) in drinking water for 7 days



D. McDall

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TITLE: Anti-CSF-1 (3)

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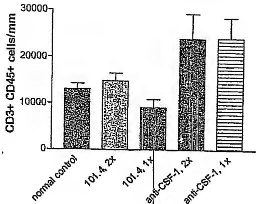
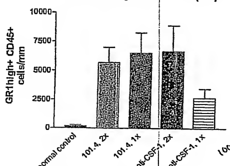
CD3+ CD45+ cells/mm in LP population from colons of mice on day 8, after DSS (1%)



GR1high+ CD45+ cells/mm in LP population from colons of mice on day 8 after DSS (1%)



10015850/62 D. McDonald

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BY	..../..../....	RECORDED BY D. McDonald	DATE

REDACTED

TITLE: anti CSF-1 (3)

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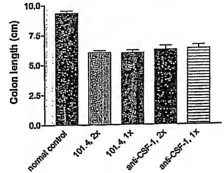
Effect of anti-CSF-1 Ab on colon length of mice after addition of DSS (1%) in drinking water for 7 days



D. McDonald 10015850/63

(CSF-1,3).pzm:Data Table-2

	A	B	C	D	E
	101.4, 2x	101.4, 1x	normal control	anti-CSF-1, 2	anti-CSF-1, 1
	Y	Y	Y	Y	Y
1	5.70	6.30	9.0	5.40	5.90
2	5.40	5.60	6.6	5.00	5.10
3	6.50		10.0	5.30	6.40
4	7.00	5.20	9.8	8.80	5.70
5	5.70	5.70	8.6	7.00	6.00
6	5.90	5.00	9.8	8.80	7.10
7	6.80	5.80	8.4	6.80	6.30
8	6.00	6.60	9.6		6.00
9	6.10	6.70	10.0	8.00	6.60
10	5.20	7.00	9.8	5.90	8.70

D. McDonald 10015850/63

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Cage 1 - DSS + 101.4

mouse weights

day	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	26.3	21.7	25.3	24	26.1	27.4	22.1	25.3	24.2	24.4	24.87	1.795036	0.568065
1	26.6	21.9	25.6	24.1	26.6	27.6	22.4	25.8	25.2	24.4	25.03	1.844541	0.583718
2	27.4	21.8	26	24.5	25.6	27.4	22.5	25.8	25.1	24.9	25.11	1.811353	0.573213
3	27.1	21.5	25.9	24	28.2	27.2	22.2	28.3	25	25	25.04	1.951182	0.617483
4	26.9	21.9	26.3	24.5	24.8	27.3	21.4	25.7	25.4	25.3	25.05	1.762731	0.557826
5	24.8	20.7	25.2	23.8	22.6	25.4	22.3	24	24.8	24.1	23.73	1.475014	0.469777
6	21.5	18	23.3	23.4	20.5	23.4	21.2	22.1	24.7	22.5	22.12	1.945022	0.615768
7		10.5	23.0	23.1		21.4	22	20.8	25.3	20.8	21.7125	2.622214	0.830131
8											#DIV/0!	#DIV/0!	#DIV/0!
9											#DIV/0!	#DIV/0!	#DIV/0!
10											#DIV/0!	#DIV/0!	#DIV/0!
11											#DIV/0!	#DIV/0!	#DIV/0!
12											#DIV/0!	#DIV/0!	#DIV/0!

DSS + 101.4

day	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	26.5	24.2	23.4	24.3	25.7	24.7	28.2	25.3	26.8	22.9	25.18	1.815756	0.511315
1	27.2	24.6	24.1	25.3	28.5	25.1	28.8	25.4	26.7	23.9	25.68	1.68937	0.534201
2	27.2	24.4	24	25	28.3	25.1	28.7	25.5	26.9	22.9	25.8	1.70815	0.540554
3	27.6	25.5	24.5	25.2	26.6	25.7	29.5	20.2	27	23.2	26.1	1.737015	0.549941
4	25.7	25.1	24.5	25.1	28.3	29.6	29.8	25.6	26.7	22.9	25.81	1.747029	0.552457
5	26.3	23.6	24	24.1	25	24	28.1	24.8	25.5	22.5	24.77	1.570595	0.497025
6	24	20.8	23.9	21.2	22.5	21.3	28.7	23.2	24.7	22.4	23.02	1.840169	0.582332
7	21.5		23.7	19.5	20.8	19.7	24.3	21.8	23.1	22.2	21.84444	1.676380	0.530503
8											#DIV/0!	#DIV/0!	#DIV/0!
9											#DIV/0!	#DIV/0!	#DIV/0!
10											#DIV/0!	#DIV/0!	#DIV/0!
11											#DIV/0!	#DIV/0!	#DIV/0!
12											#DIV/0!	#DIV/0!	#DIV/0!

control

day	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	23.9	25.6	21.1	23.2	20.1	24.2	22	24.3	23.1	26.3	23.24	2.290081	0.725859
1	26	26.8	22	20.4	20.7	24.8	22.9	25.6	23.7	26.7	23.94	2.365587	0.740603
2	26.2	20.8	22.1	20.0	21	25.8	23.1	28	24.2	26.7	24.28	2.37058	0.750177
3	29.9	25.9	22.3	20.3	20.9	26.5	23.8	28.3	24.6	26.9	24.46	2.682163	0.847457
4	20.7	27	22.1	20.8	21.2	26.2	23.8	26.9	24.3	27.4	24.63	2.570365	0.813407
5	26.6	20.3	21.0	20.2	20.8	25.1	23.4	26.8	24.7	27	24.35	2.611194	0.826327
6	27.2	25.2	21.8	20.5	20.8	26.1	23.8	26.5	24.9	27	24.43	2.609917	0.825923
7	27.1	20.8	22.1	20.7	21.2	26.5	23.9	27	25.1	27.0	24.76	2.622212	0.825814
8											#DIV/0!	#DIV/0!	#DIV/0!
9											#DIV/0!	#DIV/0!	#DIV/0!
10											#DIV/0!	#DIV/0!	#DIV/0!
11											#DIV/0!	#DIV/0!	#DIV/0!
12											#DIV/0!	#DIV/0!	#DIV/0!

DSS + anti-CSF-1

day	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	25.8	23.5	22.5	23.2	24.7	25	24.1	28	23.2	24.2	24.33	1.714027	0.542414
1	25.9	24.1	23	22.6	24.8	24.9	24.4	27.4	22.7	24.6	24.44	1.485639	0.470130
2	25.8	24.3	23.3	22.7	25.1	23.2	24.6	28.9	23.0	24.1	24.47	1.371982	0.434171
3	25.7	24.4	21.4	22.5	25.5	25.5	25.1	27.5	23.2	24.9	24.08	1.546332	0.489979
4	26.6	23.7	22.6	21.0	25.3	24.9	25.2	27.5	23	23.8	24.44	1.703351	0.587507
5	25	22	20.6	20.1	24.8	24.1	24.1	26.1	22.5	21.9	23.1	1.975404	0.625128
6	23.8	20.8	18.8	18.5	21.6	23.5	23.2	25.2	22.8	18.7	21.97	2.359402	0.746846
7	21.9	19		17.8	22.6	22	23.2	24.0	23.2		21.6125	2.312008	0.731952
8											#DIV/0!	#DIV/0!	#DIV/0!
9											#DIV/0!	#DIV/0!	#DIV/0!
10											#DIV/0!	#DIV/0!	#DIV/0!
11											#DIV/0!	#DIV/0!	#DIV/0!
12											#DIV/0!	#DIV/0!	#DIV/0!

DSS + anti-CSF-1

day	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	28.8	23.4	26.5	24.1	21.7	24.8	23.7	23.8	27	25.3	25.05	1.768395	0.559618
1	28.1	23.3	26.8	24.1	23.4	24.4	24.3	23.9	27.4	25.7	25.14	1.739221	0.550380
2	28.8	24.1	27.4	25.3	23.4	24.0	24.5	24.2	27.0	25.7	25.58	1.778764	0.5629
3	28.5	24	28.5	24.5	23.7	24.8	24.6	24	27.8	25.3	25.37	1.673353	0.529542
4	27.0	23.1	25	23.2	23.1	24.4	24.7	22.7	28.1	25.1	24.72	1.911253	0.604827
5	27	21.3	22.5	20.5	21.4	23	24	20	27.9	23.2	23.12	2.582333	0.817194
6	25.3	16.5		19.5	19.5	22.0	22.7		20.9	21.6	22.225	2.791185	0.883266
7	24	10.4			10	22.5	21.5		27.5	20.0	21.78571	3.300218	1.044372
8											#DIV/0!	#DIV/0!	#DIV/0!
9											#DIV/0!	#DIV/0!	#DIV/0!
10											#DIV/0!	#DIV/0!	#DIV/0!
11											#DIV/0!	#DIV/0!	#DIV/0!
12											#DIV/0!	#DIV/0!	#DIV/0!

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Cage 1 -

mouse weights

day	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	100	100	100	100	100	100	100	100	100	100	100	0	0
1	101.1407	100.9217	101.5873	100.4107	101.9157	100.7299	101.3575	102.3715	104.1322	100	101.4573	1.171485	0.370717
2	104.1025	100.9217	100.1746	102.0833	98.00429	100	101.81	101.9763	103.718	102.0492	101.8001	1.802467	0.570401
3	103.0418	99.07834	100.7778	100	100.3831	99.27007	100.4525	103.9526	103.3058	102.459	101.4721	1.814432	0.574187
4	102.2014	100.9217	104.3651	102.0833	95.01916	99.63504	101.3575	101.581	104.8587	103.6885	101.5651	2.021995	0.639036
5	93.53812	85.39171	100	99.33333	88.58004	92.70073	100.905	84.88100	102.4793	98.77049	96.35604	4.728470	1.495721
6	81.74505	82.94931	94.84127	87.5	78.54406	85.40146	95.9270	87.35178	102.0661	92.21311	89.85438	7.762373	2.456447
7		78.03687	94.44444	98.25		78.10219	99.54751	82.21344	104.5455	85.2459	89.54823	10.55372	3.339785
8	0	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0	0

animal number

day	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	100	100	100	100	100	100	100	100	100	100	100	0	0
1	102.6415	101.6529	102.9915	104.1152	100.1128	101.6154	102.1277	100.3953	100.3759	100	101.9032	1.354328	0.428585
2	103.6415	100.8264	102.5841	102.8807	102.3340	101.6154	101.773	100.7905	101.1270	100	101.6558	0.956253	0.302812
3	104.1509	105.3719	104.7009	103.7037	103.5019	104.0408	104.6098	103.5573	101.5038	101.31	103.6459	1.31299	0.415503
4	100.7547	101.719	104.7009	103.2922	102.3346	103.6437	104.0045	101.1058	100.3759	100	102.4971	1.822741	0.576817
5	99.24528	97.52066	102.5841	99.17895	97.27620	97.18599	99.64539	97.2332	95.68488	88.25320	98.38458	1.673152	0.50277
6	90.56604	85.12397	100.8547	97.2428	87.54804	88.23482	94.60085	91.6996	92.85714	97.81859	91.46252	5.189524	1.642255
7	81.13208		101.2021	80.24691	80.93305	78.75709	88.17021	88.16601	88.64211	96.94323	85.60017	7.682503	2.431172
8	0	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0		0	0	0
12	0	0	0	0	0	0	0	0	0		0	0	0

animal number

day	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	100	100	100	100	100	100	100	100	100	100	100	0	0
1	101.9608	103.9063	104.2654	100.9801	102.9851	102.4793	104.0909	105.3490	102.6974	101.5209	103.0148	1.369217	0.433288
2	100.1373	104.6075	104.7393	102.9703	104.4770	100.8116	105	106.9959	104.7018	101.5209	104.4002	1.630793	0.516603
3	105.098	105.0781	105.2133	100.485	101.99	109.5041	107.2727	108.2305	100.4935	102.2814	105.1657	2.880020	0.911401
4	104.7059	105.4808	104.7393	101.5802	105.4728	108.2645	107.2727	109.465	107.7922	104.1825	105.9348	2.241284	0.709201
5	104.3137	102.7344	103.3175	100	103.4020	107.8512	100.3838	109.485	106.9264	102.6616	104.7118	2.88764	0.907401
6	100.6667	102.3438	107.3697	101.4851	103.9801	107.8512	107.2727	109.0535	107.7922	102.6610	105.1477	2.046415	0.900704
7	108.2745	103.5156	104.7393	102.4752	105.4728	109.5041	106.1018	111.1111	100.658	104.943	108.4075	2.779826	0.879439
8	0	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0	0

animal number

day	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	100	100	100	100	100	100	100	100	100	100	100	0	0
1	100	102.5532	102.2222	101.8010	100.4049	99.6	101.2448	97.85714	97.54483	101.6529	100.5162	1.695111	0.530428
2	99.6139	103.4043	103.5556	102.2523	101.8194	101.2	102.0747	98.07143	97.41379	99.56870	100.6792	2.403259	0.785842
3	103.0880	103.0298	104	101.3514	103.2389	103	104.1494	98.21429	100.431	102.8826	102.3198	1.87609	0.5937
4	102.7027	100.8511	100.4444	98.1907	102.4291	99.6	104.5643	98.21429	98.13793	98.34711	100.4489	2.186204	0.691837
5	90.5251	93.61702	81.55558	90.54054	99.50514	98.4	100	93.21429	98.98276	90.48587	94.09283	3.517528	1.113141
6	91.89189	87.55057	83.65558	83.33333	95.54858	84	98.26556	90	98.27888	81.40496	90.19333	5.991147	1.895933
7	84.56558	80.85100		80.18018	91.49798	88	88.26556	88.57143	100		88.74077	7.01647	2.220407
8	0	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0	0

animal number

day	1	2	3	4	5	6	7	8	9	10	average	sd	sem
0	100	100	100	100	100	100	100	100	100	100	100	0	0
1	98.25175	99.57265	101.1321	100	98.73410	98.16090	102.5310	101.2712	101.4815	101.581	100.3743	1.418234	0.448000
2	100.6993	102.9915	103.3902	104.9793	98.72410	100.813	103.3785	102.5424	102.2222	101.581	102.1335	1.75777	0.560258
3	99.65035	102.5641	100	101.6500	100	100.813	103.7075	101.6949	102.983	100	101.3143	1.449621	0.458741
4	97.2028	98.71795	94.33002	99.26558	97.48035	99.10699	104.2194	98.18644	104.0741	99.20949	98.68707	3.246469	1.027383
5	84.40559	81.02684	84.80500	88.72199	88.29530	93.40593	101.2858	84.74576	103.3333	91.6996	92.10947	6.295085	1.992309
6	88.40154	83.33333		80.81288	82.27848	92.68283	95.78059		88.82903	85.37549	88.55688	6.83558	2.163102
7	83.91608	78.83748			75.94937	91.46341	88.7173		101.8519	81.42292	88.27806	8.978123	2.840549
8	0	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0	0

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BY	..../..../....	RECORDED BY	DATE

REDACTED

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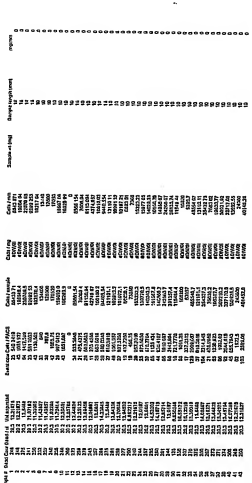
PROJECT NO

NOTEBOOK NO 1001/5856



D. McBrall 1001/5856/66

ASSESSED AND UNDERSTOOD	DATE	INVENTED BY	DATE
BY	/ /	RECORDED BY D. McBrall	DATE

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TITLE: Anki-CSF-1 (3)

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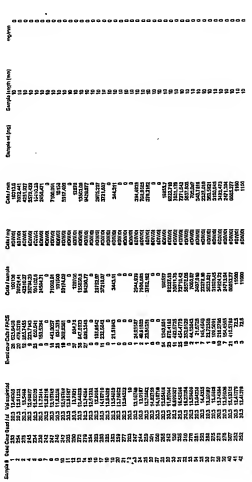

D. McBrall 1001/5856/67

ASSESSED AND UNDERSTOOD	DATE	INVENTED BY	DATE
BY	/ /	RECORDED BY D. McBrall	DATE

REDACTED